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Analysis of Static and Dynamic Host–Guest Associations of Detergents with Cyclodextrins via Photoluminescence Methods

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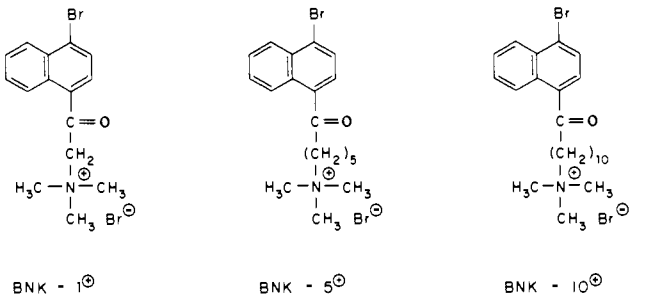
Abstract: Host–guest inclusion type associations between β- and γ-cyclodextrins (CD) and a series of cationic phosphorescence detergent probes (i.e., [*n*-(4-bromonaphthoyl)alkyl]trimethylammonium bromide, alkyl = methyl (*n* = 1, BNK-1$^+$), pentyl (*n* = 5, BNK-5$^+$), and decyl (*n* = 10, BNK-10$^+$)) are reported. No evidence for association could be detected for α-CD. The association equilibrium constant (*K*), the association rate constant (k_f), and the dissociation rate constant (k_b) were evaluated from a dynamic phosphorescence decay method by using $Co(NH_3)_6^{3+}$ as an aqueous-phase phosphorescence quencher. The k_f values are of the order of 10^7 M^{-1} s^{-1} and are independent of the detergent structure. However, the magnitudes of k_b and *K* vary over several orders of magnitude as a function of detergent and host structure. The results are discussed in terms of the importance of the dehydration of CD and/or probe as a rate-determining step of inclusion.

Cyclodextrins (CD's) possess hydrophobic cavities that are able to include, in aqueous solution, a variety of compounds whose character may vary from hydrophobic to ionic.[2] Knowledge of the mechanism of these associations is potentially of assistance for an understanding of enzyme and related kinetics. In spite of the importance of entrance/exit kinetics of the inclusion process into a cyclodextrin cavity, relatively few data on the rate constants for association (k_f) and dissociation (k_b) have been reported. The methods employed to obtain such kinetic data usually have involved temperature jump and ultrasonic relaxation methods.[3] Luminescence probes are very conveniently suited for such kinetic analysis because luminescence probes which are included in the cavity of a CD may undergo characteristic changes in their luminescence intensity, spectral distribution, and decay time.[3a,4] These changes, as well as measurements of dynamic quenching of luminescence upon inclusion, especially when such quenching is specific for the aqueous phase, can be employed to evaluate rate constants for formation and destruction of inclusion complexes and, hence, to evaluate equilibrium constants.

Scheme I



The measurement of phosphorescence decays has been employed to obtain kinetic information on the inclusion of the phosphorescent bromonaphthalene group in β-cyclodextrin.[5] We report here a novel host–guest inclusion system of β- and γ-cyclodextrins with a series of cationic phosphorescence detergent probes, i.e., [*n*-(4-bromo-1-naphthoyl)alkyl]trimethylammonium bromides, *n* = 1, 5, and 10 (Scheme I). $Co(NH_3)_6^{3+}$ was used as a dynamic phosphorescence quencher whose quenching action is confined to the aqueous phase. As a result of this selectivity, the probes included in a cyclodextrin cavity are protected from quenching by both the electrostatic repulsive interaction between the probe complex and quencher and the simple inclusion of the probe into the hydrophobic cavity.

Experimental Section

Materials. The preparations of [1-(4-bromo-1-naphthoyl)methyl]-trimethylammonium bromide (BNK-1$^+$), [5-(4-bromo-1-naphthoyl)-

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(2) For reviews, see: (a) Cramer, F. "Einschlussverbindugen"; Springer Verlag: Heidelberg, 1954. (b) Griffiths, W. D.; Bender, M. L. *Adv. Catal.* **1973**, *23*, 209. (c) Bender, M. L.; Komiyama, M. "Cyclodextrin Chemistry"; Springer Verlag: Berlin, 1978. (d) Saenger, W. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 344.
(3) (a) Cramer, F.; Saenger, W.; Spatz, H.-Ch. *J. Am. Chem. Soc.* **1967**, *89*, 14. (b) Rohrbach, R. P.; Rodriquez, L. J.; Eyring, E. M.; Wojcik, J. F. *J. Phys. Chem.* **1977**, *81*, 944. (c) Yoshida, N.; Fujimoto, M. *Chem. Lett.* **1980**, 1377.
(4) (a) Tabushi, I.; Shimokawa, K.; Shimidzu, N. Shirakawa, H.; Fujita, K. *J. Am. Chem. Soc.* **1976**, *98*, 7855. (b) Kondo, H.; Nakatani, H.; Hiromi, K. *J. Biochem.* **1976**, *79*, 393. (c) Tabushi, I.; Fujita, K.; Yuan, L. C. *Tetrahedron Lett.* **1977**, 2503. (d) Edwards, H. E.; Thomas, J. K. *Carbohydr. Res.* **1978**, *65*, 173. (e) Ueno, A.; Takahashi, K.; Osa, T. *J. Chem. Soc., Chem. Commun.* **1980**, 837, 921. (f) Kano, K.; Takenoshita, I. *Chem. Lett.* **1980**, 1035.
(5) Turro, N. J.; Bolt, J. D.; Kuroda, Y.; Tabushi, I. *Photochem. Photobiol.* **1982**, *35*, 69.

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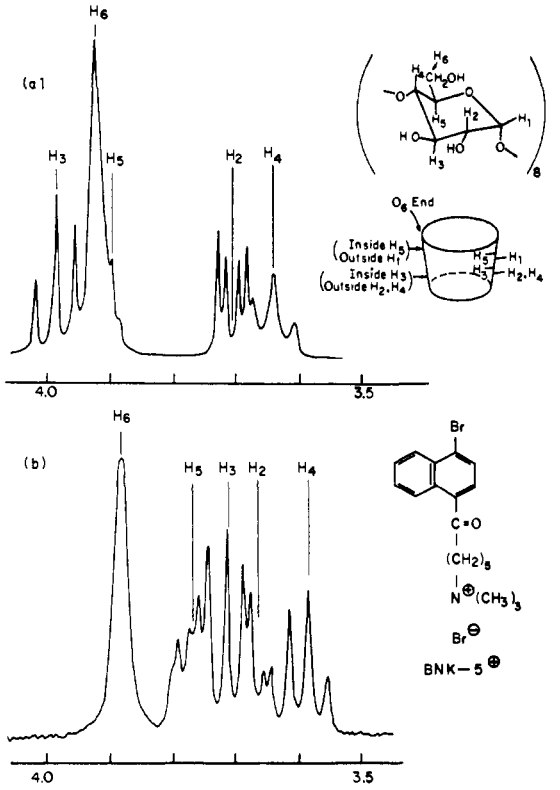


Figure 1. 300-MHz ^1H NMR spectra of γ-cyclodextrin in the (a) absence and (b) presence of BNK-5^+ in D_2O.

pentyl]trimethylammonium bromide (BNK-5^+), and [10-(4-bromo-1-naphthoyl)decyl]trimethylammonium bromide (BNK-10^+) are described in previous studies.[6] α-, β-, and γ-Cyclodextrins (Aldrich) were used as received. Hexaamminecobalt(III) chloride ($Co(NH_3)_6Cl_3$) (Alfa Products) and sodium nitrite ($NaNO_2$) were recrystallized twice from water. Phosphorescence measurements were made on solutions which were nitrogen purged 5–10 min with oxygen-free grade of N_2 (Linde).

Spectroscopy. Phosphorescence spectra were obtained on a SPEX Fluorolog Fluorimeter. Phosphorescence lifetimes were measured by using the photon-counting technique employing a pulsed source for excitation.[7,8] A Cary 118 spectrophotometer was employed to obtain absorption spectra. The ^1H NMR spectra were measured on a Bruker WN-300 MHz NMR spectrometer.

Results

^1H NMR Spectra. The H-3 and H-5 atoms of γ-CD, which are directed toward the interior of the cyclodextrin cavity,[2c] showed a significant upfield shift upon addition of BNK-5^+ to aqueous γ-CD solutions (Figure 1). This observation is consistent with the postulate that the bromonaphthyl (not the cationic) moieties interact with the H-3 and H-5 atoms.[9,10] On the other hand, the H-1, H-2, and H-4 atoms located on the exterior wall of the CD cavity showed only a marginal upfield shift (Figure 1). All the protons of BNK-5^+ were shifted downfield upon addition of BNK-5^+ to γ-CD solutions in D_2O, i.e., the methylene protons (0.5–2.5 ppm) on the side chain of BNK-5^+ were shifted downfield by 0.4 ppm, and the methyl protons of the quaternary amino group were shifted downfield by 0.2 ppm. The protons of the bromonaphthalene group also were shifted downfield. All these results suggest that BNK-5^+ is included in the cavity of γ-CD. However, beyond the question of inclusion there is the interesting issue as to the orientation of the bromonaphthyl groups, i.e., is this group buried deep in the cavity (type I inclusion) or is it close to the surface of the cavity (type II inclusion), such as the two limiting

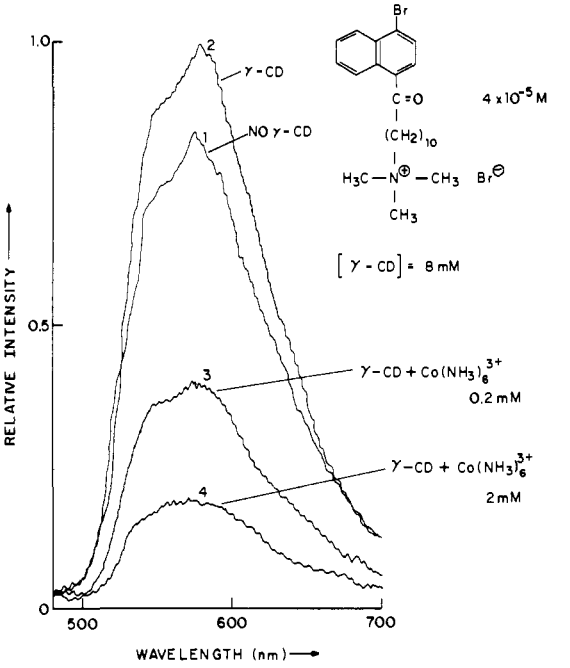
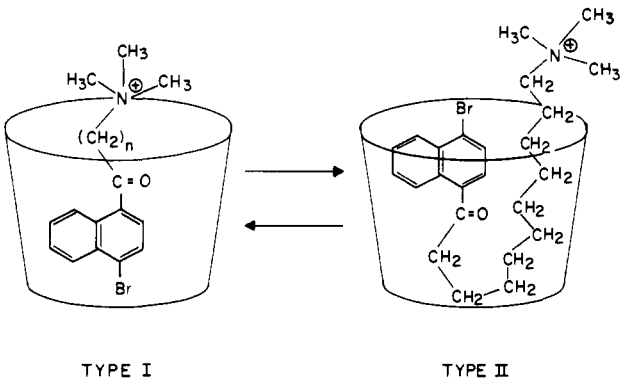


Figure 2. Phosphorescence spectra of BNK-10^+ in the presence of γ-CD and $Co(NH_3)_6Cl_3$ at 25 °C; [BNK-10^+] = 4×10^{-5} M. Curve 1, in H_2O; curve 2, [γ-CD] = 8 mM; curve 3, [γ-CD] = 8 mM, [$Co(NH_3)_6^{3+}$] = 0.2 mM; curve 4, [γ-CD] = 8 mM, [$Co(NH_3)_6^{3+}$] = 2 mM.

Scheme II



situations depicted in Scheme II?

Phosphorescence and Absorption Spectra. BNK-1^+, BNK-5^+, and BNK-10^+ all display strong phosphorescence (maximum ~ 575 nm) in N_2-purged aqueous solutions.[6,11] The effects of addition of cyclodextrin and quencher, $Co(NH_3)_6Cl_3$, on the emission of BNK-10^+ are displayed in Figure 2. The intensity of the phosphorescence was found to increase upon addition of γ-CD to aqueous solutions of the detergent probes. This result implies that the probes are associated with CD host molecules. Evidently, the quantum yield of phosphorescence is enhanced relative to that in aqueous solution by inclusion, because the nonquenching hydrophobic atmosphere around the probes provides protection from dynamic bimolecular quenching process.[7] For example, in aqueous solution, addition of $Co(NH_3)_6^{3+}$ at concentrations higher than 200 μM is sufficient to completely quench the phosphorescence of any of the probes studied. However, association of the probes with CD inhibit the quenching very effectively, i.e., strong emission was observable from DBK-10^+ in aqueous solution containing γ-CD even in the presence of 2 mM of $Co(NH_3)_6^{3+}$ (Figure 2). These observations provide further support for the postulate that the association is of the inclusion type for BNK-10^+ and γ-CD. Similar results were also obtained for the BNK-10^+ and β-CD, BNK-5^+ and β-CD, BNK-1^+ and β-CD, and BNK-1^+ and γ-CD systems. The lu-

(6) Okubo, T.; Turro, N. J. *J. Phys. Chem.* **1981**, *85*, 4034.
(7) Turro, N. J.; Liu, K.-C.; Chow, M.-F.; Lee, P. *Photochem. Photobiol.* **1978**, *27*, 523.
(8) Turro, N. J.; Aikawa, M. *J. Am. Chem. Soc.* **1980**, *102*, 4866.
(9) Demarco, P. V.; Thakkar, A. L. *Chem. Commun.* **1970**, 2.
(10) Thakkar, A. L.; Demarco, P. V. *J. Pharm. Sci.* **1971**, *60*, 652.
(11) Bolt, J. D.; Turro, N. J., submitted to *Photochem. Photobiol.*

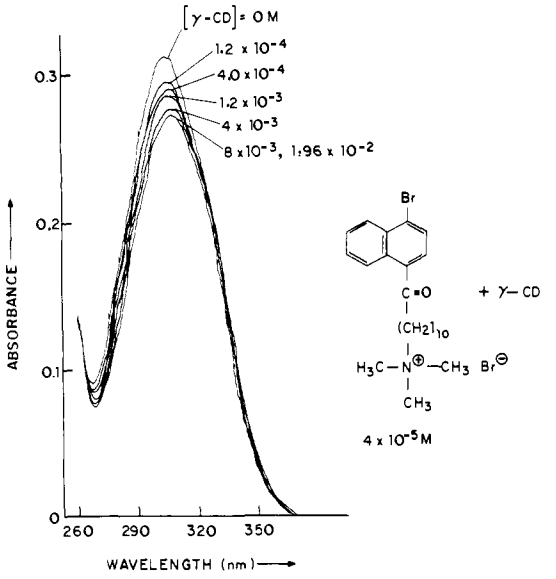


Figure 3. UV absorbance spectra of BNK-10$^+$ in the presence of γ-CD; [BNK-10$^+$] = 4×10^{-5} M, concentrations, as indicated, of γ-CD are 0, 1.2×10^{-4}, 4×10^{-4}, 1.2×10^{-3}, 4×10^{-3}, 8×10^{-3}, and 1.96×10^{-2} M.

minescence of aqueous solutions of the probes was not influenced by addition of α-cyclodextrin. Thus, the presence of CD-type molecules, per se, does not cause the striking protection from quenching observed.

The UV-absorbance spectra of BNK-10$^+$ in the presence of γ-CD at various concentrations are given in Figure 3. The absorbance maxima showed a slight red shift upon addition of γ-CD, and the extinction at the maximum decreased gradually with increasing concentration of γ-CD. From a modified Benesi–Hildebrand-type analysis,[12] i.e., optical density/[γ-CD] against optical density plots, the association constants for the BNK-10$^+$ and γ-CD complex was estimated to be $(1.4 \pm 0.5) \times 10^4$ M^{-1}. This value agrees with that estimated from the phosphorescence lifetime measurements (vide infra). For the other systems such as BNK-1$^+$ and β-CD (or γ-CD) and BNK-10$^+$ and β-CD, the changes in the absorbance of the probe with cyclodextrin addition are not large enough to allow for an accurate analysis of association constants. The absorbance spectra of aqueous solution of the probes were not influenced by the addition of α-CD.

The equilibrium association constants for the BNK-5$^+$/γ-CD and BNK-10$^+$/γ-CD systems were also determined by measurements of phosphorescence intensity as a function of [γ-CD] at fixed concentration of probe. The values of K obtained in this manner were 480 and 14 300 M^{-1} for the BNK-5$^+$ and BNK-10$^+$ probes, respectively. These values compare favorably within the ±20% estimated error limits with those obtained from quenching data (440 and 16 300 M^{-1}).

Phosphorescence Lifetimes. Typical examples of the phosphorescence decay in the presence and absence of quencher (BNK-1$^+$ and β-CD and BNK-10$^+$ and γ-CD) are given in Figure 4 and 5. For all systems studied, except the BNK-10$^+$ and γ-CD system, a single first-order relaxation upon addition of quencher was observed up to a 99% decrease in the value of the initial intensity. However, for the BNK-10$^+$ and γ-CD system, *two first-order relaxations were obtained in the presence of quencher, but phosphorescence decay was first order in the absence of quencher.* Interestingly, Figure 5 shows that the fast relaxation component is more readily quenched by $Co(NH_3)_6^{3+}$ than the longer lived component. Indeed, the slow decaying component persisted even in the presence of excess amount of $Co(NH_3)_6^{3+}$. The observation of two relaxations implies the existence of two kinds of inclusion structures possibly such as those shown in Scheme II. The phosphorescence lifetimes of the detergent probes

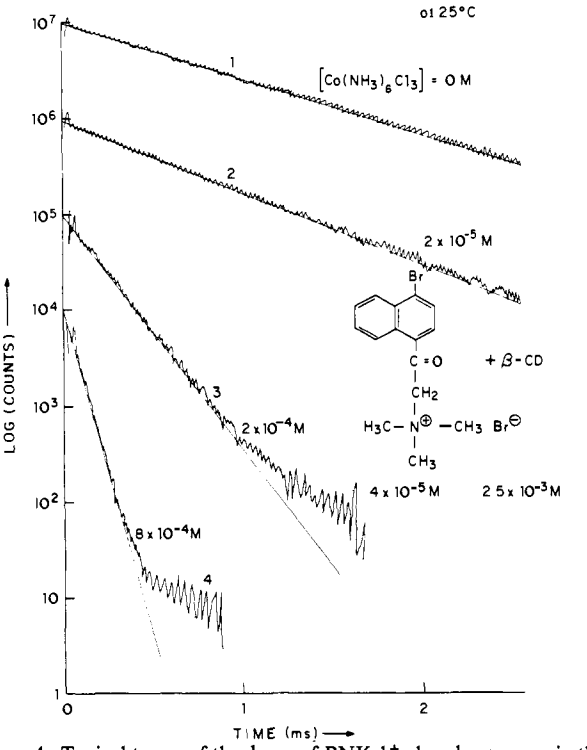


Figure 4. Typical traces of the decay of BNK-1$^+$ phosphorescence in the presence of β-CD and various concentrations of $Co(NH_3)_6Cl_3$ quencher at 25 °C; [BNK-1$^+$] = 4×10^{-5} M, [β-CD] = 2.5×10^{-3} M. Curve 1, $[Co(NH_3)_6Cl_3]$ = 0 M; curve 2, 2×10^{-5} M; curve 3, 2×10^{-4} M; curve 4, 8×10^{-4} M.

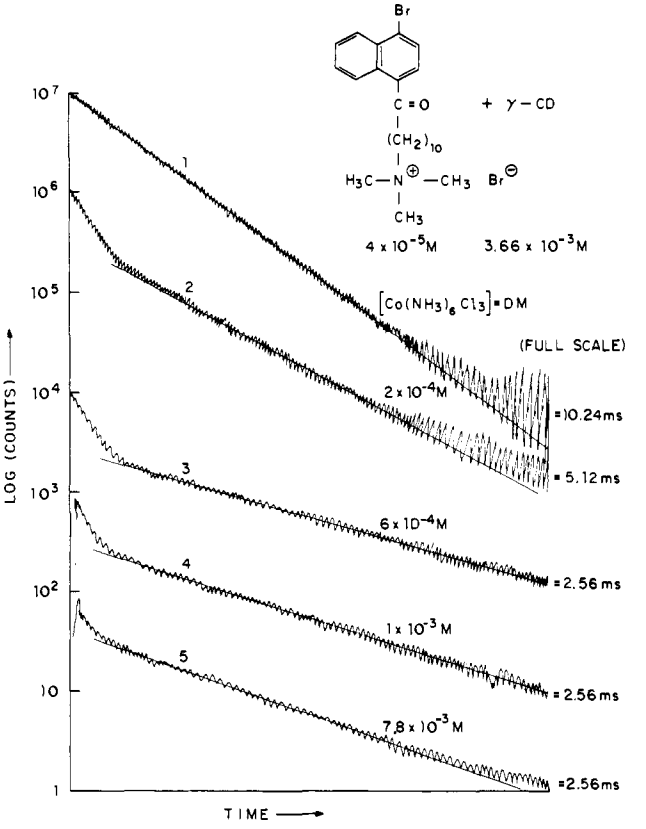


Figure 5. Typical traces of the decay of BNK-10$^+$ phosphorescence in the presence of γ-CD and $Co(NH_3)_6Cl_3$ quencher at 25 °C. [BNK-10$^+$] = 4×10^{-5} M; [γ-CD] = 3.66×10^{-3} M; curve 1, $[Co(NH_3)_6Cl_3]$ = 0 M; curve 2, 2×10^{-4} M; curve 3, 6×10^{-4} M; curve 4, 1×10^{-3} M; curve 5, 7.8×10^{-3} M.

become longer upon addition of a complexing CD. For example, the τ values of the BNK-n^+ probes are about 1 ms in pure water.

(12) Foster, R.; Hammick, D. L.; Wardley, A. A. *J. Chem. Soc.* **1953**, *75*, 3817.

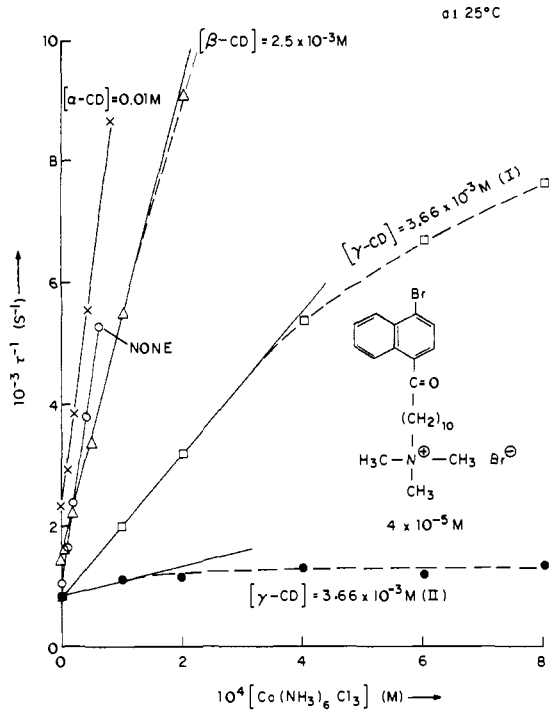


Figure 6. τ^{-1} vs. $[Co(NH_3)_6Cl_3]$ plots for BNK-10$^+$ in H_2O (O), α-CD (X; 0.01 M), β-CD (Δ; 2.5×10^{-3} M), γ-CD ($\square$; 3.66×10^{-3} M assigned to type I inclusion, and γ-CD ($\bullet$; 3.66×10^{-3} M assigned to type II inclusion at 25 °C. [BNK-10$^+$] = 4×10^{-5} M.

However, values between 1.2 and 1.8 ms are observed in the presence of γ-CD.

Figure 6 shows τ^{-1} vs. [quencher] plots for BNK-10$^+$ in the presence of the three cyclodextrins. From the slopes of these plots the apparent quenching rate constant, $k_{q,obsd}$ may be evaluated and compared to the value of the quenching constant in pure water, $k_{q,0}$. The ratio $k_{q,obsd}/k_{q,0}$ serves as a qualitative parameter for the strength of the inclusional forces between probe and CD. The ratios were 1.15, 0.57, 0.15, and 0.017 for the systems of BNK-10$^+$ with α, β, γ (short-lived), and γ (long-lived), respectively, when $Co(NH_3)_6^{3+}$ is used as quencher. The decrease in the ratio of $k_{q,obsd}/k_{q,0}$ means that the triplets are protected from the attack of the quencher and provides a qualitative measure of the protection afforded to the bromonaphthyl moieties that are included into the cavity of β- or γ-cyclodextrin.

Determination of Kinetic Parameters. In order to extract the kinetic parameters for the inclusion reactions, the reaction given in the reaction scheme shown in (1) are considered. The processes

$$\begin{array}{ccc} T + CD & \underset{k_b}{\overset{k_f}{\rightleftharpoons}} & T{\cdot}CD \\ k_w \downarrow \; k_q[Q] & & k_{CD} \downarrow \; k_q'[Q] \\ \text{no T} & & \text{no T} \end{array} \qquad (1)$$

listed in reaction 1 lead to the expression for the observed rate constant, k_{obsd}, given in eq 2. In eq 2, k_w and k_{CD} represent the

$$k_{obsd} = \tau^{-1} = k_b + k_{CD} + k_q'[Q] - \frac{k_f k_b [CD]}{k_f[CD] + k_w + k_q[Q]} \qquad (2)$$

triplet deactivation rate constants in water and the CD complex, respectively. The reaction scheme is completely analogous to the association–dissociation processes between phosphorescence probes and micelles.[8,13] As in the case for quenching of probes in ionic micelles by quenchers with the same charge as the micelle surface, cationic quenchers, $Co(NH_3)_6^{3+}$, are repelled from the cationic CD inclusion complex by electrostatic forces; as a result, the $k_q'[Q]$ term in eq 2 is assumed to be negligibly small compared with the $k_q[Q]$ term.

(13) Almgren, M.; Grieser, F.; Thomas, J. K. *J. Am. Chem. Soc.* **1979**, *101* 279.

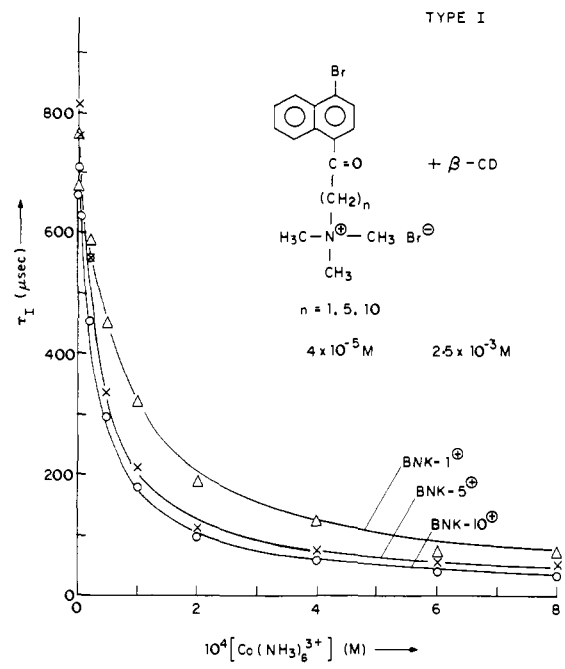


Figure 7. τ^{-1} vs. $[Co(NH_3)_6Cl_3]$ plots for BNK-1$^+$ and β-CD (Δ), BNK-5$^+$ and β-CD (X), and BNK-10$^+$ and β-CD (O) systems at 25 °C. [BNK-n^+] = 4×10^{-5} M; [β-CD] = 2.5×10^{-3} M.

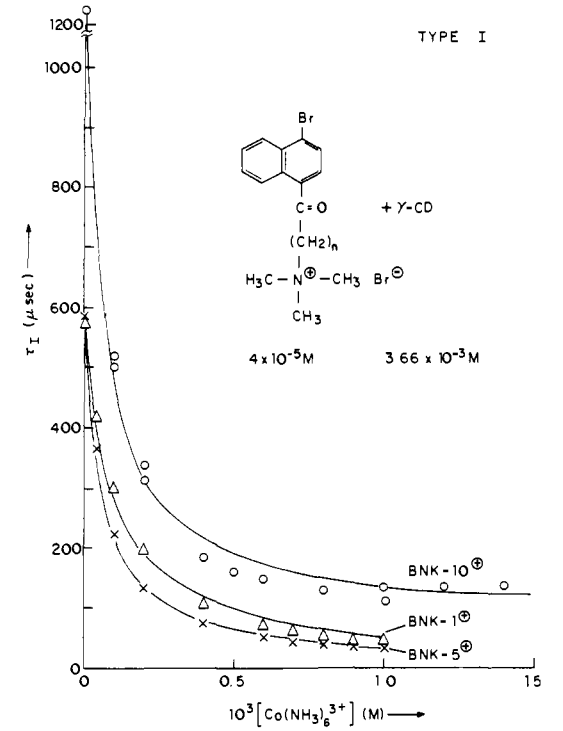


Figure 8. τ^{-1} vs. $[Co(NH_3)_6Cl]$ plots for BNK-10$^+$ and γ-CD (O), BNK-5$^+$ and γ-CD (X), and BNK-1$^+$ and γ-CD (Δ) systems at 25 °C. [BNK-n^+] = 4×10^{-5} M; [γ-CD] = 3.66×10^{-3} M.

The various parameters of eq 2 were determined by computer simulation of experimental data.[13] In addition, the qualitative values of K (association constant) were derived independently from the equation, $K = k_{q,0}/k_{q,obsd}[CD]$ at low concentrations of quencher. Typical results for quenching are seen in Figures 7, 8, and 9. The solid curves are the calcualted values from eq 2 into which the fitting parameters of Table I have been inserted. We view the agreement between the experimental values of lifetimes and the calculation as satisfactory.

To obtain further information concerning the strength of the association between BNK-10$^+$ and γ-CD, we employed an anionic quencher, NO_2^-, for the kinetic analyses (Figure 10). Indeed,

Table I. Equilibrium and Kinetic Constants of the Host-Guest Complexation of BNK-1$^+$, BNK-5$^+$, and BNK-10$^+$ with α-, β-, and γ-Cyclodextrins[a]

host	guest	$k_{q,obsd}/k_{q,o}$	K, M^{-1}	$10^{-7}k_f$, M^{-1} s^{-1}	k_b, s^{-1}	$10^{-7}k_q$, M^{-1} s^{-1}	k_w, s^{-1}	k_{CD}, s^{-1}
α-CD[b]	BNK-1$^+$	1.00	0			2.6	1550	
	BNK-5$^+$	0.92	0			5.3	1040	
	BNK-10$^+$	1.15	0			7.2	1020	
β-CD[b]	BNK-1$^+$	0.68	700	3.5	50 000	2.6[f]	1550	500
	BNK-5$^+$	0.64	520	2.2	42 000	5.3[f]	1040	500
	BNK-10$^+$	0.57	590	2.4	40 000	7.2[f]	1020	750
γ-CD[b]	BNK-1$^+$	0.67	360	1.5	42 000	2.6[f]	1550	500
	BNK-5$^+$	0.54	440	1.9	43 000	5.3[f]	1040	1100
	BNK-10$^+$[c]	0.12	2360	1.3	5 500	6.7	840	450
	BNK-10$^+$	0.15	1300	1.5	12 000	7.2	1020	600
	BNK-10$^+$[g]	0.23	920	1.2	13 000	260	1020	750
	BNK-10$^+$[d]	0.18	850	1.7	20 000	8.2	1190	800
	BNK-10$^+$[c,e]	0.0067	30000	0.8	270	6.7	840	570
	BNK-10$^+$[e]	0.017	16300	1.3	800	7.2	1020	800
	BNK-10$^+$[e,g]	0.081	4800	1.0	2 100	260	1020	750
	BNK-10$^+$[d,e]	0.0071	11000	1.7	1 550	8.2	1190	1550

[a] Except where noted, the temperature of the experiment was 25 °C, the quencher was $Co(NH_3)_6^{3+}$. The error limits are estimated to be no larger than ±20% in any of the measurements. [b] [α-CD] = 0.1 M; [β-CD] = 0.0025 M; [γ-CD] = 0.004 M. [c] T = 15 °C. [d] T = 35 °C. [e] Measurements refer to the long-lived emission observed in Figure 5. [f] In these cases, k_q' is estimated to be ~3 × 10^6 M^{-1} s^{-1}. For the other entries $k_q' << k_b + k_{CD}$. [g] The quencher was NO_2^-.

Table II. Thermodynamic Parameters for the Complexation of BNK-10$^+$ with γ-Cyclodextrin at 25 °C

type	ΔG, kcal/mol^{-1}	ΔH, kcal/mol^{-1}	ΔS, eu	$\Delta G^{\ddagger}_f$, kcal/mol^{-1}	$\Delta H^{\ddagger}_f$, kcal/mol^{-1}	$\Delta S^{\ddagger}_f$, eu	$\Delta G^{\ddagger}_b$, kcal/mol^{-1}	$\Delta H^{\ddagger}_b$, kcal/mol^{-1}	$\Delta S^{\ddagger}_b$, eu
I	−4.3	−9.0	−16	7.7	1.8	−20	11.9	10.8	−4
II	−5.8	−9.0	−11	7.8	5.9	−7	13.6	14.9	4

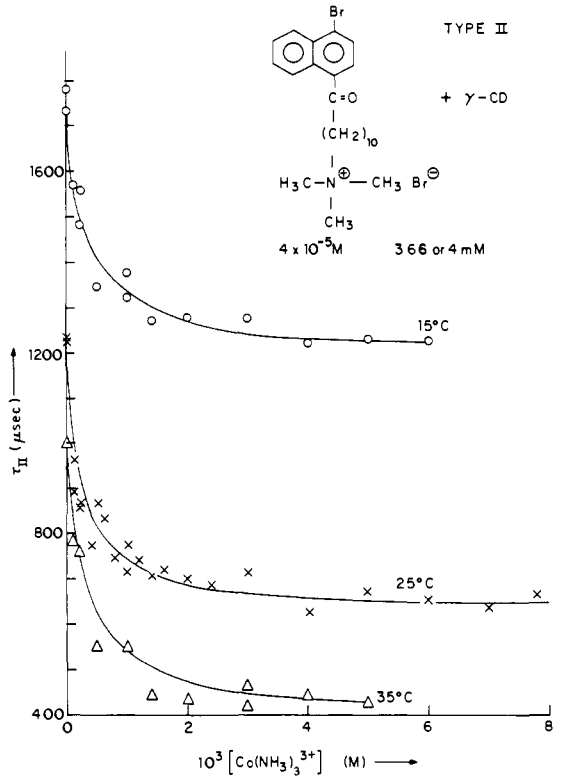


Figure 9. τ^{-1} vs. $[Co(NH_3)_6Cl_3]$ plots for BNK-10$^+$ and γ-CD systems (type II) at 15 (○), 25 (×) and 35 °C (△). [BNK-10$^+$] = 4 × 10^{-5} M; [γ-CD] = 3.66 mM (25 °C), 4 × 10^{-3} M (15, 35 °C).

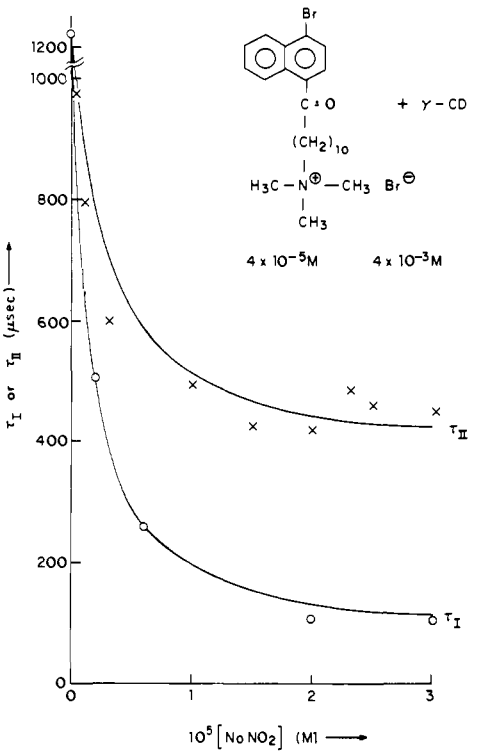


Figure 10. τ^{-1} vs. $[NaNO_2]$ plots for BNK-10$^+$ and γ-CD systems at 25 °C. (○) type I; (×) type II. [BNK-10$^+$] = 4 × 10^{-5} M; [γ-CD] = 4 × 10^{-3} M.

the BNK-10$^+$'s phosphorescence with γ-CD was protected strongly even from the attack of NO_2^-. This result is consistent with a predominance of an association of BNK-10$^+$ with γ-CD that is not only strong but is also structurally protective, in spite of the attractive nature of the cationic complex toward anions, i.e., this is evidence for a complex of type II structure (Scheme II). As is clear in Table I, when NO_2^- was used as a quencher, the smaller values of K and k_f and the larger value of k_b were estimated rather than those obtained when $Co(NH_3)_6^{3+}$ quencher was used. This is expected because the $k_q'[Q]$ term in eq 2 can no longer be neglected and an accurate analysis using eq 2 is no longer possible.

It should be noted that the association constants (K) given in Table I vary between 440 and 30000 M^{-1}. The high K value found for BNK-10$^+$ and γ-CD system, i.e., 16300 M^{-1} at 25 °C, was quantitatively confirmed by independent absorption (and phosphorescence) measurements which yield values of K = 14000 and 14300 M^{-1}, respectively. The strength of complexation with γ-CD

increased in the order of BNK-1$^+$ < BNK-5$^+$ < BNK-10$^+$. Importantly, all k_f values obtained were of the order of 10^7 M^{-1} s^{-1}. The latter value is below that for the diffusion-controlled reaction and is rather insensitive to the system involved. On the other hand, k_b was sensitive to the detergent and CD structure and was found to vary between 270 and 50 000 s^{-1}.

From temperature dependencies of K, k_f, and k_b of BNK-10$^+$ and γ-CD system, the free energies (ΔG, $\Delta G^{\ddagger}_f$ and $\Delta G^{\ddagger}_b$), enthalpies (ΔH, $\Delta H^{\ddagger}_f$ and $\Delta H^{\ddagger}_b$), and entropies (ΔS, $\Delta S^{\ddagger}_f$, and $\Delta S^{\ddagger}_b$) of the complexation reaction and activation were derived (Table II). The values of ΔH and ΔS estimated here are similar to those reported previously for the various kinds of inclusion reactions of CD.[3a,14]

Discussion

The bromonaphthyl group is too large to be inserted into the cavity of α-CD (4.5 Å in diameter). Further, the overall size of the quaternary ammonium groups is slightly larger than that of the α-CD's cavity. Thus, no inclusion of α-CD with any of our probes is expected and is experimentally confirmed. ^{1}H NMR measurements support the inclusion of the detergent probes into the inner cavity of γ-CD. The type I inclusion (Scheme II) of the bromonaphthyl group into the cavity explains the quenching results. In general, the cationic group may be placed outside and cover the cavity. The postulate that the size of bromonaphthyl group is small enough to be included in the cavity of β- or γ-CD but not in the cavity of α-CD is supported also by the low values of $k_{q,obsd}/k_{q,0}$.

A type of complexation that is different from type I is required to explain the data for the system of BNK-10$^+$ and γ-CD. The association constant for this system is exceptionally high, 16 300 M^{-1} (at 25 °C). A molecular model shows that the BNK-10$^+$ molecule in a folded form fits in the cavity of γ-CD. In this case, the naphthyl and carbonyl parts are buried entirely in the cavity and the bromine atom, and the cationic group are located outside the cavity. The differential quenching of the two emissions observed for BNK-10$^+$ in γ-CD (Figure 5) may be associated with either a more effective quenching due to a differential reactivity of the Type I and Type II complexes or a different equilibrium concentration of the two complexes or some combination of both factors. At this point we speculate that it is the escape rate that determines the probe triplet lifetimes. Thus the type I structure dissociates faster than the type II structure for BNK-10$^+$.

As is seen in Table I, the strength of complexation increases in the order BNK-1$^+$ < BNK-5$^+$ < BNK-10$^+$ for γ-CD (Type I). This order is consistent with an important role of hydrophobic interactions in the course of inclusion. As is clear further from Table I, all k_f values were of the order of 10^7 M^{-1} s^{-1} and are quite insensitive to the inclusion system. On the other hand, k_b varied significantly between 270 and 50 000 s^{-1}. These facts suggest that the rate-determining step of the host–guest association is the breakdown of the water structure inside CD and/or around probe. The important role of the dehydration to the association process was discussed earlier by Cramer et al.[3a]. Finally, it should be noted that, strictly speaking, our data applies to *triplet* probes and not to ground-state probes. The results are expected to be representative of ground-state behavior because of the nonpolar nature of the triplet of the BNK moiety.

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Registry No. [*N*-(4-Bromo-1-naphthoyl)methyl]trimethylammonium bromide, 80214-62-6; [*N*-(4-bromo-1-naphthoyl)pentyl]trimethylammonium bromide, 79671-16-2; [*N*-(4-bromo-1-naphthoyl)decyl]trimethylammonium bromide, 79671-17-3; α-cyclodextrin, 10016-20-3; β-cyclodextrin, 7585-39-9; γ-cyclodextrin, 17465-86-0; α-CD-BNK-1$^+$ complex, 80800-13-1; α-CD-BNK-5$^+$ complex, 80800-14-2; α-CD-BNK-10$^+$ complex, 80822-20-4; β-CD-BNK-1$^+$ complex, 80800-15-3; β-CD-BNK-5$^+$ complex, 80800-16-4; β-CD-BNK-10$^+$ complex, 80822-21-5; γ-CD-BNK-1$^+$ complex, 80800-17-5; γ-CD-BNK-5$^+$ complex, 80800-18-6; γ-CD-BNK-10$^+$ complex, 80822-22-6.

(14) (a) Van Etten, R. L.; Clowes, G. A.; Sebastian, J. F.; Bender, M. L. *J. Am. Chem. Soc.* **1967**, *89*, 3242. (b) Straub, T. S.; Bender, M. L. *Ibid.* **1972**, *94*, 8881. (c) Lewis, E. A.; Hansen, L. D. *J. Chem. Soc., Perkin Trans. 2* **1973**, 2081.

(15) It was found from conductance measurements that the hydrocarbon moieties of sodium dodecylsulfate and hexadecyltrimethylammonium bromide are included into the cavities of α-, β-, and γ-CD. See ref 16.

(16) Okubo, T.; Kitano, H.; Ise, N. *J. Phys. Chem.* **1976**, *80*, 2611.

Proton Affinity and Ion–Molecule Reactions of a Simple Silyl Enol Ether

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Abstract: The gas-phase positive ion–molecule chemistry of the simple silyl enol ether, 2-(trimethylsiloxy)propene (**1**), has been studied by using ion cyclotron resonance spectroscopy. A lower bound to the proton affinity (PA) of **1** is found to be 16 ± 1 kcal/mol above PA(NH_3). The experimental results are consistent with C-protonation forming an ion with a structure equivalent to that of the adduct of the trimethylsilyl cation with acetone. The reactivity of the protonated enol ether suggests that most of the positive charge is localized on the trimethylsilyl group. This is in agreement with molecular orbital calculations on a model complex. On the basis of thermochemical data, the protonated enol ether is calculated to be stable by 42 ± 10 kcal/mol with respect to the trimethylsilyl cation and acetone. Trimethylsilyl cation transfer reactions to various bases B have been observed from both the adduct and protonated **1**. A dual group transfer reaction involving transfer of a proton from BH^+ to **1** and abstraction of the trimethylsilyl cation by the base to form the products B–$SiMe_3^+$ and acetone has been observed to occur in a single reactive encounter. A brief comparison with solution results is made.

Silyl enol ethers are among the most commonly used organosilicon reagents.[1] For the most part, however, the mechanisms of their chemical reactions have not been systematically studied.[2] Among the mechanistic questions that remain poorly defined are (1) the factors that govern the site of electrophilic attack on silyl

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(1) Rasmussen, J. *Synthesis*, **1977**, 91.

0002-7863/82/1504-1794$01.25/0